Mortality in Critically Ill Elderly Individuals Receiving Mechanical Ventilation

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BACKGROUND: Previous studies that evaluated mortality in elderly subjects who received mechanical ventilation had conflicting results. The aim of this systematic review was to evaluate the effects of age on mortality. **METHODS:** A number of medical literature databases and the references listed (from 1974 to May 2015) were searched for studies that compared 2 different age groups. The primary outcome was mortality in subjects ages ≥ 65 y. The severity scores, ICU and hospital lengths of stay, and the presence of ventilator-associated pneumonia were secondary outcomes. Finally, mortality in the subjects with ARDS and of cutoff ages 70 and 80 y was assessed by subgroup analysis. Evidence quality was assessed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria score. **RESULTS:** Of the 5,182 articles identified, 21 were included. Subjects ages ≥ 65 y had higher mortalities (odds ratio [OR] 1.80, 95% CI 1.56–2.08; $I^2 = 71\%$). APACHE (Acute Physiology and Chronic Health Evaluation) II revealed intergroup differences (mean difference 3.07, 95% CI 2.52–3.61; $I^2 = 0\%$), whereas neither the ICU nor hospital length of stay (mean difference 1.27, 95% CI -0.82 to 3.36 , $I^2 = 82\%$, and mean difference 1.29, 95% CI -0.71 to 3.29 , $I^2 = 0\%$, respectively) nor the groups in the 2 studies that assessed ventilator-associated pneumonia exhibited any difference. Subgroup analysis revealed a higher mortality in the older subjects, in the subjects with ARDS (OR 1.76, 95% CI 1.30–2.36; $I^2 = 0\%$) and in the subjects ages 70 and 80 y (OR 1.78, 95% CI 1.51–2.10, $I^2 = 71\%$; and OR 1.96, 95% CI 1.81–2.13, $I^2 = 0\%$, respectively). The quality of associated evidence was low or very low. **CONCLUSIONS:** Although low-quality evidence was available, we conclude that age is associated with a greater mortality in critical subjects who were receiving mechanical ventilation. *Key words:* elderly; mechanical ventilation; intensive care unit; outcome; age; systematic review. [Respir Care 2019;64(4):473–483. © 2019 Daedalus Enterprises]

Introduction

In recent decades, the proportion of the population > 60 y old has steadily increased. These demographic changes

resulted in higher admission rates to ICUs of elderly patients. Current estimations indicate that two thirds of all bed-days in ICUs in the developed world have been allocated to patients ages > 65 y.¹ Moreover, in certain countries, such as Australia and New Zealand, between 10 and

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15% of the ICU beds are occupied by patients >80 y.² Because these patients have a high requirement for mechanical ventilation, the impact of this intervention on mortality deserves considerable evaluation. The existing evidence regarding elderly patients on ventilation has not yet allowed definitive conclusions to be drawn.

Although some studies indicated that age had a detrimental effect on the outcomes of subjects who received mechanical ventilation,^{2,3} other studies revealed no association.^{4,5} Moreover, most of the studies available are observational, in which data are not adjusted for confounders and included subjects with a wide range of pathologies (ie, with case mix). Therefore, we conducted a systematic review and meta-analysis to evaluate the mortality rate of subjects in the ICU ages ≥ 65 y who received mechanical ventilation compared with subjects ages < 65 y. Moreover, in the meta-analysis conducted, the subjects with ARDS or with higher cutoff points for age were also considered.

Methods

The protocol was registered on PROSPERO (Centre for Reviews and Dissemination University of York, York, UK; CRD42015020568) in October 2015, and, subsequently, updated in October 2017. The systematic review was conducted according to the checklist of the Meta-analysis of Observational Studies in Epidemiology group.⁶ A systematic search was performed in (May 2015) MEDLINE (National Library of Medicine 8600 Rockville Pike, Bethesda, Maryland), Cochrane Central Register of Controlled Trials (Rigshospitalet, Copenhagen Denmark), and Embase (Elsevier BV Registered Office, Amsterdam, The Netherlands). We used a strategy that combined key words and descriptors (Medical Subject Headings or Embase Subject Headings) without language restriction. In addition, we screened the reference list of all the available review articles and primary studies. We also searched www.clinicaltrials.gov for ongoing studies and set the similar-articles option in PubMed (see the supplementary materials at <http://www.rcjournal.com>).

We included observational studies that compared 2 different age groups in the evaluation of mortality in subjects who were receiving mechanical ventilation while in an ICU. No language restrictions were imposed on the study selection. We excluded studies that compared subjects of different ages in the ICU but with missing mechanical ventilation data. Two of us (RSC and FV) screened all the studies from the databases for eligibility based on the titles and abstracts. Each of us selected some of the citations that were suspected to meet the eligibility criteria for the review. On identifying a citation as potentially relevant, one of us (RSC or FV) obtained the full article for review in detail to decide on that article's inclusion or exclusion.

Disagreements were resolved by consultation with a third author (AF), who then made the decision on a study's inclusion or elimination. We removed duplicates. One of us (RSC) contacted investigators of the studies reviewed for clarification and retrieval of reported and unreported relevant data. In some studies that included 3 comparative groups, the cutoff point for the age for inclusion in the study in the different subgroups was performed by one of us (RSC) on the basis of the characteristics of the study.

The data extraction was performed through the use of a prespecified data-extraction form. For each study, we detailed the following when present: characteristics of the study design, the inclusion criteria in relation to age, the selection of the groups for comparison, the number of subjects in each age group, and the presence of confounding factors. We also evaluated the following variables: severity scores, length of stay in both the ICU and the hospital, and the presence of ventilator-associated pneumonia. The primary outcome was to determine mortality in subjects ages ≥ 65 y who received mechanical ventilation in the ICU compared with subjects ages < 65 y. We aimed to report hospital mortality; but, if that information was not present, then we considered mortality in the ICU. The secondary outcomes were to determine severity scores, lengths of stay in the ICU, lengths of stay in the hospital, and the presence of ventilator-associated pneumonia. Also, according to the statement in the Cochrane Handbook⁷ for the primary outcome of mortality, we performed the following subgroup analysis: subjects with ages 65 y as a cutoff point with ARDS⁸ and subjects ages 70 and 80 y as the cutoff point.

Assessments of the methodological quality of the studies included in the primary outcome were performed by 2 of us (RSC and FV). We used 26 of the 27 items on the checklist of Downs and Black.⁹ Item 27, which is related to power, was extracted from a modified version of this checklist.¹⁰ This checklist comprises the assessment of the differences among subjects in different intervention groups (ie, the selection bias); the distribution of principal confounders; and the presence of performance, detection, and attrition biases.¹⁰ The scale of the overall score ranges from 0 to 29. The scores were also expressed as percentages.¹¹ Scores between 80 and 100% are considered very good, 70 and 79% are good, and those between 50% and 69% are considered fair.¹¹ We assessed the quality of the body of evidence associated with the outcomes according to the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria guidelines.¹² We also investigated whether an adjustment was made for confounders in each of the studies included.¹³

We combined the studies through a meta-analysis. Odds ratio (OR) measurements at a 95% CI were used as estimates of the relationship between the older and younger subjects, this parameter being the appropriate statistic when

Fig. 1. Flow chart.

the logistic regression is used to adjust for confounding factors. The variation in the results of the studies was evaluated by drawing a forest plot, whereas the statistical heterogeneity was assessed by the I^2 test at a 95% CI,¹⁴ thereby estimating the percentage of total variance among studies that was attributable to heterogeneity rather than to chance.¹⁵ When no significant statistical heterogeneity was found ($I^2 < 20\%$), the fixed-effect model was used; whereas, when I^2 was $\geq 20\%$, (which indicates moderate-to-high levels of heterogeneity), a random-effects model was used. In secondary outcomes, for continuous data, we use mean difference. All statistical analyses were performed with Review Manager version 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark).

Results

Identification of the Studies

The flow diagram depicted in Figure 1 delineates the process used for the identification of the eligible studies. Of the 5,182 citations, after discarding the duplicates and revising the abstracts, we identified 61 potentially relevant studies. No ongoing studies were found. One study was in Chinese and required translation.¹⁶ During the evaluation of the full text of the articles, 40 studies were discarded. Finally, on the basis of a quantitative synthesis, 21 studies were included (11 studies included in the primary outcome plus 10 studies included in the subgroup analysis).

Primary Outcome

All the studies included were cohort studies, 6 were retrospective,^{16–21} and 5 were prospective.^{22–26} Three stud-

ies compared several groups according to age and, subsequently, to perform the meta-analysis, these groups were divided into 2 groups, with an age cutoff point of 65 y.^{19,21,23} Four studies contained only subjects with ARDS.^{16,22,25,26} The control group was variable in age among the studies. In 2 studies, the ages were between 45 and 64 y.^{16,18} In another study, the ages were between 55 and 64 y;²³ and, in the rest of the studies, all the subjects were <64 y old. The characteristics of the studies included are summarized in Table 1.

As evaluated according to the checklist of Downs and Black,⁹ 10 studies averaged between 50 and 69% (a fair study quality)^{16–23,25,26}; one averaged between 70 and 79% (a good study quality).²⁴ All 11 studies reported on mortality,^{16–26} 7 reported on hospital mortality,^{17,20,21,23–26} and 5 reported on ICU mortality.^{16,18,19,22,24} We pooled all those studies and used a random-effects model because the I^2 value was 71%. The subjects ages ≥ 65 y were found to have a higher mortality than those younger than that cutoff age (OR 1.80, 95% CI 1.56–2.08; $P < .001$ (Fig. 2).

Sensitivity Analysis

To assess the robustness of the primary outcome, we performed sensitivity analyses and separated the studies that registered hospital mortality from those studies that recorded mortality in the ICU. We evaluated hospital mortality in 7 studies and by using a random-effects model because the I^2 was 72%, found a statistically significant difference between the 2 groups (OR 1.90, 95% CI 1.60–2.26; $P < .001$ (see supplementary materials at <http://www.rcjournal.com>).^{17,20,21,23–26} We then evaluated ICU mortality in 5 studies^{16,18,19,22,24}; and with the random-effects model likewise being used because the I^2 was 40%, we also obtained a statistically significant difference between the 2 groups (OR 1.47, 95% CI 1.18–1.83, $P < .001$ (see supplementary materials at <http://www.rcjournal.com>). The quality of the evidence and strength of the recommendation (ie, GRADE) for these 3 outcomes were ranked as very low (Table 2).

Secondary Outcomes

Severity Scores. The scores used were the following: APACHE II,²⁷ APACHE III,²⁸ Simplified Acute Physiology Score II,²⁹ and Acute physiology score (the score considered the acute physiologic variables included in the Simplified Acute Physiology Score II or APACHE III). We pooled 3 studies that used APACHE II (which trials included means $\pm$ SDs), used the fixed-effect model because the I^2 statistic was 0%, and found statistically significant differences between the 2 groups (mean difference 3.07, 95% CI 2.52–3.61, $P < .001$ (Fig. 3)).^{16,18,24}

Table 1. Characteristics of the Studies Included in the Primary Outcome

Study	Study Design	Subjects, Age Groups: <i>n</i>	Checklist of Downs and Black*	Case Mix	Adjusting for Confounding	Observations
Blot et al ¹⁹	Retrospective multicenter	Group 45–64 y: 670; group 65–74 y: 549; group ≥75 y: 516	19	Yes	Yes	NA
Douglas et al ¹⁷	Retrospective single center	Group 45–64 y: 421; group ≥65 y: 700	17	Yes	No	The authors state that 16.1% of the middle-age subjects had advance directives and were terminally weaned compared with 20.9% of the older subjects ($P = .27$)
Duke et al ²⁰	Retrospective single center	Group <65 y: 54,191; group ≥65 y: 49,912	16	Yes	No	NA
Eachempati et al ²²	Prospective single center	Group <65 y: 133; group ≥65 y: 210	18	Yes	No	The authors state that older subjects had a higher percentage of “do not resuscitate” orders written vs young subjects (29.6 vs 14.9%, $P = .002$)
Farfel et al ²³	Prospective single center	Group 55–64 y: 147; group 65–74 y: 195; group ≥75 y: 140	20	NR	Yes	The authors state that a selection bias on ICU admission could have occurred
Feng et al ²¹	Retrospective single center	Group <65 y: 1,884; group ≥65 y: 2,354	19	NR	Yes	NA
Li et al ¹⁶	Retrospective single center	Group <65 y: 72; group ≥65 y: 78	18	NR	No	NA
Sodhi et al ¹⁸	Retrospective single center	Group <65 y: 298; group >65 y: 352	18	NR	Yes	The authors state that, in the study, treatment limitations probably differed according to age
Suchyta et al ²⁵	Prospective single center	Group < 65 y: 156; group ≥65 y: 59	17	NR	No	NA
Tang et al ²⁴	Prospective single center	Group <65 y: 159; group ≥65 y: 206	22	Yes	Yes	The authors state that they could have selected those elderly subjects for ICU admission who otherwise were in good physical condition
Zilberberg and Epstein ²⁶	Prospective single center	Group <65 y: 76; group ≥65 y: 31	20	NR	No	NA

* From Reference 9.
 NA = not applicable
 NR = not reported

Fig. 2. Primary outcome. Forest plot of comparisons between subjects ≥ 65 y and subjects < 65 y. Mortality, sensitivity analysis: hospital mortality, and sensitivity analysis: ICU mortality.

Length of Stay in the ICU. In this meta-analysis, we pooled 3 studies and used the random-effects model because the I^2 statistic was 82%, and found no statistically significant differences between the 2 groups (mean difference 1.27 d, 95% CI, -0.82 to 3.36 d; $P = .23$ (Fig. 3)).^{17,18,24}

Length of Stay in the Hospital. In this meta-analysis, we pooled 2 studies, used the fixed-effect model because the I^2 statistic was 0% and, likewise, obtained no statistically significant differences between the 2 groups (mean difference 1.29 d, 95% CI, -0.71 to 3.29 d; $P = .21$) (Fig. 3)).^{17,24}

The quality of the evidence and the strength of the recommendation (ie, GRADE) for these 3 outcomes (severify scores, length of stay in the ICU, and length of stay in the hospital) were ranked as low or very low (Table 2).

Ventilator-Associated Pneumonia. We could not pool data for the meta-analysis of this variable and thus as-

sessed the presence of ventilator-associated pneumonia as a number and the percentage of the total in the age group. Blot et al¹⁹ compared 3 groups and found no differences: subjects ages ≥ 75 y, 73 (14.1%); subjects ages 65–74 y, 104 (18.9%); and subjects ages 45–64 y, 103 (15.4%); $P = .08$. Eachempati et al²² likewise found no significant difference between the groups: subjects ages ≥ 65 y, 144 (68.4%); and subjects ages < 65 y, 86 (64.7%); $P = .69$.

Subgroup Analysis

Subjects Ages ≥ 65 y and With ARDS Compared With Subjects Ages < 65 y and With ARDS. Four studies were pooled.^{16,22,25,26} Two studies reported hospital mortality,^{25,26} and 2 studies reported ICU mortality.^{16,22} In this meta-analysis, the use of a fixed-effect model, because I^2 was 0%, revealed a statistically significant difference between the 2 groups (OR 1.76, 95% CI 1.30–2.36; $P < .001$ (Fig. 4)).

Table 2. Quality of the Body of Evidence Associated With the Outcomes According to GRADE

Study Type: No. of Studies	Certainty Assessment					Subjects		Effect Relative (95% CI)	Certainty
	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Elderly n, dead/total (%)	Younger n, dead/total (%)	
Mortality: 11	Observational studies	Serious*	Serious†	Not serious	Not serious	None	14,408/55,302 (26.1)	7,976/58,207 (13.7)	OR 1.80 (1.56–2.08) ND
Sensitivity analysis; hospital mortality: 7	Observational studies	Serious‡	Serious§	Not serious	Not serious	None	13,674/53,597 (25.6)	7,606/57,034 (13.3)	OR 1.90 (1.90–2.26) ⊕○○○ Very low
Sensitivity analysis; ICU mortality: 5	Observational studies	Not serious	Serious	Not serious	Not serious	None	803/1,911 (42)	426/1,332 (3.9)	OR 1.47 (1.18–1.83) ⊕○○○ Very low
Secondary outcome: APACHE II: 3	Observational studies	Not serious	Not serious	Not serious	Not serious	None	1,500	1,332	MD 3.07 (2.52–3.61) ⊕⊕○○ Low
Secondary outcome: length of stay in the ICU: 3	Observational studies	Not serious	Serious	Not serious	Not serious	None	2,122	1,681	MD 1.27 (–0.82 to 3.36) ⊕○○○ Very low
Secondary outcome: length of stay in the hospital: 2	Observational studies	Serious¶	Not serious	Not serious	Not serious	None	906	580	MD 1.29 (–0.71 to 3.29) ⊕○○○ Very low
Subgroup analysis: subjects ages ≥65 y with ARDS compared with subjects ages <65 y and with ARDS: 4	Observational studies	Serious**	Not serious	Not serious	Not serious	None	224/378 (59.2)	210/437 (48)	OR 1.76 (1.30–2.36) ⊕○○○ Very low
Subgroup analysis: subjects ages ≥70 y compared with subjects ages <70 y: 6	Observational studies	Serious††	Serious‡‡	Not serious	Not serious	None	13,825/23,463 (58.9)	10,981/24,552 (44.7)	OR 1.78 (1.51–2.10) ⊕○○○ Very low
Subgroup analysis: subjects ages ≥80 y compared with subjects ages <80 y: 4	Observational studies	Serious§§	Not serious	Not serious	Not serious	None	1,528/3,143 (48.6)	4,545/13,572 (33.4)	OR 1.96 (1.81–2.13) ⊕○○○ Very low

* In 6 of the included studies, no adjustment for confounders.

† Substantial heterogeneity (71%).

‡ In 3 of the included studies, no adjustment for confounders.

§ Substantial heterogeneity (72%).

|| Moderate heterogeneity (40%).

¶ In one of the included studies, no adjustment for confounders (the study of greater weight).

** In 3 of the included studies, no adjustment for confounders.

†† In 5 of the included studies, no adjustment for confounders.

‡‡ Substantial heterogeneity (71%).

§§ In all included studies, no adjustment for confounders.

GRADE = Grading of Recommendations Assessment, Development, and Evaluation

ND = no data

OR = odds ratio

MD = mean difference

○○○ Symbol used to represent grading system.

MORTALITY IN OLDER MECHANICALLY VENTILATED INDIVIDUALS

Fig. 3. Secondary outcomes. APACHE II, ICU length of stay, and hospital length of stay.

Fig. 4. Subgroup analysis. Forest plot of comparisons between older and younger subjects. Subjects with ARDS, and subjects with 70 and 80 y of age as cutoff points.

Subjects Ages ≥ 70 y Compared With Subjects Ages < 70 y. Six studies were included.³⁰⁻³⁵ For this meta-analysis, 4 studies^{31,32,34,35} reported hospital mortality, one study³³ reported ICU mortality, and one study³⁰ reported mortality at 28 d. By using the random-effects model, because I^2 was 71%, we found a statistically significant difference between the 2 groups (OR 1.78, 95% CI 1.51–2.10; $P < .001$) (Fig. 4).

Subjects Ages ≥ 80 y Compared With Subjects Ages < 80 y. In this analysis, according to the outcomes presented in the studies included, we considered hospital mortality. Four studies were pooled, and the fixed-effect model was used because the I^2 statistic was 0%, and statistically significant differences were found between the 2 groups (OR 1.96, 95% CI 1.81–2.13; $P < .001$) (Fig. 4).³⁶⁻³⁹

The quality of the evidence and strength of the recommendation (ie, GRADE) for these 3 outcomes (subjects ages ≥ 65 y and with ARDS compared with subjects ages < 65 y and with ARDS; subjects ages ≥ 70 y compared with subjects ages < 70 y; and subjects ages ≥ 80 y compared with subjects ages < 80 y) were ranked as very low (Table 2). The characteristics of the studies included in the subgroup analysis are summarized in Table 3.

Discussion

This review found that the mortality rate of subjects ages ≥ 65 y who received mechanical ventilation in ICUs was significantly higher than in younger subjects. With regard to secondary outcomes, the stay in the ICU and in the hospital, as well as the presence of ventilator-associated pneumonia, were not different between the groups, albeit elderly subjects had a higher APACHE II score. A subgroup analysis that compared elderly with younger subjects and that evaluated different age limits, including one comparison between patients with ARDS, also revealed a higher mortality in the older subjects. Despite these results, the evidence as assessed by the GRADE, was considered very low. In addition, for the primary outcome, only one study reached a good quality score (according to the checklist of Downs and Black⁹),²⁴ and several of the studies involved case mix.^{17,19,20,22,24} For this reason, we also need to emphasize that the inadequate methodological quality of the available evidence with respect to mortality in elderly subjects who received mechanical ventilation prevented us from drawing definitive conclusions.

We evaluated only subjects who received mechanical ventilation because we considered that mechanical ventilation was a determining element in the prognosis of elderly patients. Certain studies found mechanical ventilation to be a risk factor associated with mortality in subjects ages ≥ 65 y,⁴⁰ in subjects ages ≥ 80 y,⁴¹ in elderly sub-

jects with trauma,⁴² or in older subjects with acute ischemic stroke and who are critically ill.⁴³ In addition, 2 of the studies included in this review that separated elderly subjects according to the mechanical-ventilation requirement concluded that higher mortality occurred in the subjects who received mechanical ventilation.^{18,23} Therefore, the mechanical-ventilation requirement placed an additional weight of risk in the prognosis of mortality in elderly patients, a conclusion in concordance with the outcomes of our review, in which we found increased mortality in elderly subjects who received mechanical ventilation.

For the primary outcome, we accordingly found a higher mortality of subjects in the ICU and ages ≥ 65 y, in accordance with what has been shown in other studies of subjects who either received prolonged mechanical ventilation⁴⁴ or had blunt trauma.⁴⁵ We must emphasize here that, when we performed a sensitivity analysis by separating the studies that registered hospital mortality from those that recorded mortality in the ICU, we consistently found the same result. In addition, in subjects with ARDS, the result of the 4 studies included in the subgroup analysis also indicated a higher mortality in the elderly subject group.^{16,22,25,26} Our findings, therefore, were consistent with previous reports on cohorts of subjects with ARDS as well as with a systematic review that found an association between age and mortality.⁴⁶⁻⁴⁸

Certain investigators indicated that the stay in the ICU and in the hospital are similar in young and elderly patients,^{49,50} an observation that was consistent with the results garnered in this review but differed from the difference obtained specifically in ICU mortality. A possible explanation for this discrepancy could be that mechanical ventilation stabilizes and homogenizes patients in the acute phase of a disease but does not modify the impact of the severity of the disease, the underlying comorbidities, or the physiologic limitations in response to injury, as has likewise been proposed by other investigators.^{17,38}

We used the APACHE II as a marker of disease severity and found that the score was increased in elderly patients. For that reason, consistent with previous findings,^{51,52} we considered that the general prognosis in elderly patients mainly depends on the severity of the illness. It should be noted that Vosylus et al,⁵³ in a study that assessed the determinants of outcome in elderly subjects admitted to the ICU, in which the Simplified Acute Physiology Score II was included, considered that a greater level of severity of illness is directly related to increasing points assigned to elderly subjects in the Simplified Acute Physiology Score II and other scoring systems. In addition, Knaus et al⁵⁴ found that only 3.4% of the predictive power of mortality in the APACHE III system was attributed to age. All these elements support the idea that APACHE II would mainly be associated with the severity of the disease.

Table 3. Characteristics of the Studies Included in the Subgroup Analysis

Study	Study Design	Subjects, Ages Groups: <i>n</i>	Severity Scores Grouped by Ages		Case Mix	Adjusting for Confounding	Observations
			Grouped by Ages, (mean $\pm$ SD)	<i>P</i>			
Cohen and Lambrinos ³⁴	Retrospective multicenter	Group <70 y: 20,494; group $\geq$ 70 y: 21,354	NR	ND	NR	No	ND
Ely et al ³⁰ (patients with ARDS)	Retrospective multicenter	Group <70 y: 729; group $\geq$ 70 y: 173	NR	ND	Yes	Yes	ND
Esteban et al ³¹	Retrospective multicenter	Group <70 y: 2,506; group $\geq$ 70 y: 1,612	SAPS II, <70 y: 44 $\pm$ 17; $\geq$ 70 y: 49 $\pm$ 16	.02	Yes	No	The authors state that selection bias could have occurred on the use of mechanical ventilation, selection of a subgroup of elderly subjects with a good prognosis, and differences in rates of "do not resuscitate" orders or withdrawal of life support
Papadakis et al ³²	Retrospective multicenter	Group <70 y: 474; group $\geq$ 70 y: 138	NR	ND	NR	No	The authors state that, in the study, there was selection bias on ICU admission
Pesau et al ³⁵	Retrospective single center	Group <70 y: 266; group $\geq$ 70 y: 99	NR	ND	No	No	ND
Rodriguez-Regañón et al ³³	Prospective multicenter	Group <70 y: 83; group $\geq$ 70 y: 87	SAPS II, <70 y: 39 $\pm$ 16 $\geq$ 70 y: 49 $\pm$ 15	<i>P</i> = < .01	Yes	No	The authors state that, in the study, there was a increased use of withdrawal or withholding of life support in older subjects (9% vs 3%; <i>P</i> = .07); the authors also state that selection bias could have occurred on ICU admission and that the study may have selected a subgroup of elderly subjects with a good prognosis
Andersen and Kvåle ³⁶	Retrospective multicenter	Group <80 y: 11,782; group $\geq$ 80 y: 2,815	NR	ND	NR	No	The authors state that, in the study, could have occurred withhold/withdrawal of life support; they also state that, in the study, selection bias could have occurred on ICU admission
Benhamou et al ³⁷	Retrospective single center	Group <80 y: 48; group $\geq$ 80 y: 10	SAPS, <80 y: 6.1 $\pm$ 2.5; $\geq$ 80 y: 7.2 $\pm$ 3	<i>P</i> = < .01	Yes	No	The authors state that in the study could have occurred selection bias on ICU admission
Chertcoff et al ³⁸	Prospective single center	Group <80 y: 164; group $\geq$ 80 y: 36	APACHE II, <80 y: 21.3 $\pm$ 9.8; $\geq$ 80 y: 28.7 $\pm$ 10.1	<i>P</i> = < .0003	Yes	No	The authors state that, in the study, selection bias on ICU admission and on use of MV could have occurred
Swinburne et al ³⁹	Retrospective single center	Group <80 y: 1578; group $\geq$ 80 y: 282	NR	ND	Yes	No	The authors state that, in the study, selection bias on the use of mechanical ventilation could have occurred

NR = not reported

ND = no data

SAPS = Simplified Acute Physiology Score

APACHE = Acute Physiology and Chronic Health Evaluation

The main strength of this review was that the exhaustive screening of the relevant literature involved a high-sensitivity systematic search of the main available databases without language restriction through the use of standardized techniques. For this reason, we believed that the studies included in this review constituted all the evidence on the assessment of elderly subjects in the ICU who received mechanical ventilation that was readily available up to the moment of carrying out the literature search.

There were limitations of this review. First, in the primary outcome, 8 studies^{17,19,20–22,24–26} included subjects in the control group ages 18 to 64 y; therefore, the selection may have generated an additional bias because a comparison between more homogeneous populations (ie, subjects ages ≥ 45 y) would have been preferable. Second, we used hospital or ICU mortality because short-term survival may clearly benefit from ICU treatment (in this instance, through the use of mechanical ventilation). Certain authors, however, considered that the assessment of mortality at 6 months or a year was probably a more appropriate end point.^{55,56} Third, 3 studies involved an increased use of withdrawal or withholding of life support,^{17,22,33} although, in 2 of these studies,^{17,33} the degree of withdrawal was balanced between the groups. In contrast, Eachempati et al²² reported a higher percentage of cases that involved do not resuscitate orders in older subjects; this could modify the outcomes. For this reason, the conclusions drawn should, nevertheless, be regarded with some degree of caution. Fourth, due to the cutoffs in relation to age (which was specified in the protocol), some important studies with different cutoff points may have been excluded from the review. However, according to the results obtained, we believed that there would be no significant changes.

Conclusions

This review found that the mortality rates in elderly subjects who received mechanical ventilation, with special emphasis on those ages ≥ 65 y, were higher than in younger subjects, although the quality of the evidence remained low. Our analysis supports the notion that the requirement for mechanical ventilation and the severity of illness, and not the patient's age, are decisive elements in the prognosis of elderly patients. The intensification of research on the treatment of this growing population of older patients in the ICU, and especially those who require mechanical ventilation, along with an improvement in the evidence quality will lead to better informed decisions in managing elderly patients in the ICU.

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